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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Elizabeth Jaffee

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EXAMINER

GUSSOW, ANNE

ART UNIT

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1643

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/618,088	Applicant(s) JAFEE ET AL.	
	Examiner Anne M. Gussow	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26, 38, 115 and 122-126 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26, 38, 115 and 122-126 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 26, 38, and 115 have been amended.
Claims 1-25, 27-37, 39-114, and 116-121 have been cancelled.
Claims 122-126 have been added.
2. Claims 26, 38, 115, and 122-126 are under examination.
3. The following office action contains NEW GROUNDS of Rejection.
4. The examiner apologizes for the confusion regarding the finality of the previous office action. The previous office action was non-final.

Rejections Maintained/ NEW GROUNDS of Rejection

Claim Objections

5. Claim 126 is objected to because of the following informalities: the claims do not recite proper Markush language. Applicant is required to amend the claims to be a proper Markush group, for example "selected from the group consisting of..."
Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 26, 38, 115, 122, 123, and 126 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite for reciting the phrase "...Listeria monocytogenes bacterium which expresses a first polypeptide..." in the amended claims. The claims do not recite a second or subsequent polypeptide. It is not clear what the bacterium is expressing in the absence of second or subsequent polypeptides.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 26, 38, 115, and 122-126 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed November 13, 2009 has introduced NEW MATTER into the claims. Newly amended claims 26, 38, and 115 and newly added claims 122, 123, and 126 recite the limitation "first polypeptide". Newly added claims 124 and 125 recite the limitation "wherein the first polypeptide is fused to a second polypeptide". The response

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pointed to paragraph 44 of the specification for support of the newly added claims.

Paragraph 44 discloses specific lengths (8-25 amino acid residues) of polypeptides for immunization. Paragraph 44 does not support the expression of a first and second polypeptide from a *Listeria monocytogenes* bacterium. The instant claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in newly amended claims 26, 38, and 114 and newly added claims 122-126, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The rejection of claims 26, 38, and 115, and newly added claim 126 under 35 U.S.C. 103(a) as being obvious over Weiskirch and Paterson (Immunological Reviews,

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1997) in view of Argani, et al. (Clinical Cancer Research, 2001) and Quan, et al. (Disease-a-Month, 1997) is maintained.

Applicant's arguments and declaration filed November 13, 2009 have been fully considered but they are not persuasive. The response states that the data in Table 2 of the specification show that for human patients that did not generate a DTH2 response to mesothelin the average survival time was 18.5 months. In contrast, the patients that did generate such a response survived for greater than 60 months. This is a remarkable improvement in the survival of patients with an otherwise grim prognosis. The data in Figure 11 show similarly remarkable results in a mouse model. Under conditions where none of the mice survived beyond 20 days post-challenge, 60 % of the mice inoculated with a mesothelin expressing construct survived greater than 90 days post-challenge. Thus the life-prolonging effect of an immune response to mesothelin is robust. Due to the general inability in the art to treat this disease effectively, these clinical and laboratory results are certainly unexpected in their magnitude. (see response pages 4-8).

In response to this argument, while the examiner agrees that the treatment of cancer is complex for the reasons set forth below at the very least it would have been obvious for one of ordinary skill in the art to try to induce a T-cell response to a tumor by administering an MHC-1 binding epitope of mesothelin because Argani, et al. teach that mesothelin is overexpressed in a number of cancer types and that it has been shown to be a promising target for immunotherapy for those malignancies (page 3862, 2nd column). Also, regarding applicants argument that immune tolerance would prevent the

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induction of an immune response, since the instant binding epitope would be expressed by a bacterial cell (the instant method administers a *Listeria monocytogenes* bacterium), one of ordinary skill in the art would presume that the MHC cells would not recognize the peptide as a self peptide (thus having immune tolerance) because the peptide was introduced from a bacterial cell.

Further, the declaration under 37 CFR 1.132 filed November 13, 2009 is insufficient to overcome the rejection of claims 26, 38, and 115 and newly added claim 126 as set forth in the last Office action because: the declaration appears to be attempting to assert unexpected results, however, the declaration focuses on a number of unrelated protein molecules (e.g. PSCA, EGFR). Although some patients may exhibit immunological tolerance to a mesothelin therapy, there is no evidence in applicant's declaration, or in the references of Weiskirch and Paterson or Argani to suggest that one of ordinary skill in the art should not have used mesothelin epitopes to induce a T-cell response to a tumor. Applicant's focus on the effect of a delayed type hypersensitivity response (DTH) however, it is noted that the features upon which applicant relies (i.e., DTH) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For each of these reasons the references provide one of ordinary skill in the art with a reasonable expectation of success that the administration of a mesothelin MHC-1 binding epitope would provide a therapeutic benefit. Applicant is reminded that

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obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976).

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP § 2145 generally for case law pertinent to the consideration of applicant's rebuttal arguments.

In the instant case since Weiskirch and Paterson teach the administration of a *Listeria Monocytogenes* bacterium interferon for induction of an MHC class I immune response and Argani, et al. teach that mesothelin is overexpressed in a number of cancer types and has been used as a target for immunotherapy, one of ordinary skill in the art would be motivated to and have a reasonable expectation of success to have used the bacteria of Weiskirch and Paterson to induce a T-cell response with the mesothelin protein of Argani, et al.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Conclusion

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
January 25, 2010

/Anne M. Gussow/
Examiner, Art Unit 1643

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643